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Total Number of Pages in This Submission: 22

Application Number	10/705,926
Filing Date	November 13, 2003
First Named Inventor	Pavel SLANINA et al.
Art Unit	1624
Examiner Name	Susanna MOORE
Attorney Docket Number	SYN-0036

ENCLOSURES *(Check all that apply)*

- [x] Fee Transmittal Form
  - [x] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please Identify below):
  Return receipt postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Synthon IP Inc.		
Signature			
Printed name	Mark R. Buscher		
Date	November 5, 2007 (Monday)	Reg. No.	35,006

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name	Mark R. Buscher	Date	November 5, 2007 (Monday)

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Effective on 12/08/2004.
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FEE TRANSMITTAL For FY 2008

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT	($)	510.00

Complete if Known	
Application Number	10/705,926
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Examiner Name	Susanna MOORE
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METHOD OF PAYMENT (check all that apply)

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES Fee ($)	FILING FEES Small Entity Fee ($)	SEARCH FEES Fee ($)	SEARCH FEES Small Entity Fee ($)	EXAMINATION FEES Fee ($)	EXAMINATION FEES Small Entity Fee ($)	Fees Paid ($)
Utility	310	155	510	255	210	105	
Design	210	105	100	50	130	65	
Plant	210	105	310	155	160	80	
Reissue	310	155	510	255	620	310	
Provisional	210	105	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	210	105
Multiple dependent claims	370	185

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 20 or HP =	_____ x	_____ =	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 3 or HP =	_____ x	_____ =	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims Fee ($)	Multiple Dependent Claims Fee Paid ($)
_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $260 ($130 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
_____ - 100 =	_____ / 50 =	_____ (round up to a whole number) x	_____ =	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other (e.g., late filing surcharge): Filing a Brief in support of an Appeal	510.00

SUBMITTED BY			
Signature		Registration No. (Attorney/Agent) 35,006	Telephone 703-753-5256
Name (Print/Type)	Mark R. Buscher		Date November 5, 2007 (Monday)

PATENT
SYN-0036

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Pavel SLANINA et al.	:	
Serial No.: 10/705,926	:	Group Art Unit: 1624
Confirm. No.: 7713	:	Examiner: Susanna MOORE
Filed: November 13, 2003	:	

For: PROCESS FOR MAKING RISPERIDONE AND INTERMEDIATES THEREFOR

APPEAL BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Further to the Notice of Appeal filed September 4, 2007, appellants hereby submit the Appeal Brief in connection with the above-identified application. The required Appeal Brief fee is attached. Entry and consideration of this Brief are requested. For the reasons set forth hereinafter, reversal of each of the Examiner's rejections is respectfully requested.

Table of Contents

I. Real Party in Interest

The real party in interest is Synthon IP Inc., a corporation of Virginia, which is one of several privately held companies ultimately owned by Synthon Holding BV, a corporation of The Netherlands.

II. Related Appeals and Interferences

There are no appeals or interferences, previously or currently, that are related to this application.

III. Status of Claims

Claims 1-9, 12, and 13 are pending in the application, wherein:

Claims 1-9 and 13 are rejected.

Claim 12 is objected to.[1]

Claims 10, 11, and 14-39 have been cancelled.

IV. Status of Amendments

An Amendment under 37 C.F.R. 1.116 was filed on September 4, 2007, and was entered into the written record by the Examiner as indicated in the Advisory Action dated September 27, 2007. Accordingly, the claims as amended "After Final" are attached in the Claims Appendix.

[1] Claim 12 now depends from claim 10 – a cancelled claim. Claim 12 should have been amended to depend from claim 9 when claim 9 was amended to incorporate the limitations of cancelled claim 10. Applicants will amend claim 12 to correct its dependency once prosecution is resumed.

V. Summary of Claimed Subject Matter

Applicants discovered that although oximes (3) and (7) are formed as a mixture of Z and E geometric isomers in the prior art synthetic schemes, essentially only the Z-isomer cyclizes to a benzisoxazole ring in risperidone synthesis. See the instant Specification at page 6, lines 1-3. Because of the discovery that the E-isomer is not merely slower reacting than the Z-isomer but rather is essentially unreactive, the less the amount of the E-isomer oxime content, the more advantageous and productive the synthetic pathway is made. *Id.* at page 7, lines 7-10. Thus, a method of producing risperidone can be enhanced by providing an enriched Z-isomer oxime. *Id.* at page 6, lines 8-9.

This surprisingly led to the discovery that the Z- and E-isomer oxime can be readily separated from one another when converted into an acetic acid salt form. *Id.* at page 6, lines 6-13. Thus, conveniently, an acetic acid salt can be used to provide an enriched Z-isomer oxime. *Id.* at page 7, lines 14-15. For example, an acetic acid salt of the Z-isomer oxime of formula (3) or (7) can be preferentially precipitated from a solution containing a mixture of the Z- and E-isomer oximes. *Id.* at page 7, lines 15-17. The precipitation is "preferential" in that the precipitate, generally crystalline material, contains a higher Z:E ratio than the solution. *Id.* at page 7, lines 17-18. The form of the acetic acid salt is not limited and specifically includes solid state forms such as crystalline forms. *Id.* at page 8, lines 20-21.

Independent claim 1 is directed to an acetic acid salt of a compound of formula (3) or (7). Support for claim 1 can be found throughout the instant specification, e.g., at

page 4, lines 10-14, page 5, lines 9-11, page 6, lines 9-12, page 7, lines 14-17, page 8, lines 17-18, page 9, lines 6-9, Examples 1 and 2, and original claim 1.

Independent clam 9 is directed to an enriched Z-isomer oxime of formula (3) or (7), in which the amount of the Z-isomer is at least 95% based on the total amount of the oxime. Support for claim 9 can be found throughout the instant specification, e.g., at page 5, lines 3-5, page 7, lines 5-7, page 15, lines 3-5, Examples 1-4, and original claims 9-11.

VI. Grounds of Rejection to be Reviewed on Appeal

Whether claims 9 and 13 are anticipated by Marquillas Olondriz (ES 2050069) under 35 U.S.C. § 102(b).

Whether claims 1-8 would have been obvious over Strupczewski (U.S. 4,408,054) under 35 U.S.C. § 103(a).

VII. Arguments

A. Claims 9 and 13 are not anticipated by Marquillas Olondriz

Claims 9 and 13 stand rejected under 35 U.S.C § 102(b) as allegedly being anticipated by Marquillas Olondriz, ES 2050069 (hereinafter "Olondriz")[2]. This rejection is in error and reversal thereof is requested.

Independent claim 9 recites an enriched Z-isomer oxime of formula (3) or (7), wherein the amount of Z-isomer accounts for at least 95% of the oxime; e.g., at least 95% of the Z- and E-isomer mixture is Z-isomer. The Examiner asserts that such an enriched

[2] While this Spanish Patent is written the Spanish language, no English translation is of record. The Examiner is fluent in Spanish.

Z-isomer oxime of formula (7) is found in Olondriz's Example 10, based on the high yield/efficiency reported for its conversion to risperidone.

Specifically, Example 10 of Olondriz shows cyclization of an oxime of applicants' formula (7) to make risperidone using sodium hydride as the base in tetrahydrofuran (THF). Carrying out the reaction for one hour at reflux (per the Examiner approx. 68°C), caused 0.1089 g (or 0.2532 mol) of oxime (7) to be converted to 88 mg of risperidone, for a yield of 84.7%. Because applicants teach that essentially only the Z-isomer reacts in the cyclization reaction and because no reaction is perfectly efficient, the Examiner reasons that Olondriz must have had at least 95% of Z-isomer oxime in the starting oxime of (7) in order to achieve 84.7% yield. But the Examiner's guess is unreasonable in view of the data of record.

Example 6 in the present application shows that 99% of the Z-isomer of oxime (7) cyclizes to risperidone in one hour using aqueous potassium hydroxide as the base in ethanol at a temperature of 80°C. Similarly, Example 8 shows that cyclizing Z-isomer of oxime (7) for only 30 minutes at only 70°C results in a 94.7% yield. That is, 50 g of oxime (7) produced 45.26 g of product. Assuming that the Z-isomer oxime used in Examples 6 and 8 was 100% pure, then the reaction is highly efficient (e.g. 94-99%).

Olondriz's Example 10 could not have inherently possessed at least 95% Z-isomer. If 95% of the oxime (7) was the Z-isomer form, and such Z-isomer converts in 94% efficiency, then Example 10 should have yielded (0.95)(0.94)(.2532 mols of oxime (7)) or 0.226 moles of risperidone. This translates to 92 mg of risperidone[3]. But Olondriz only achieved 88 mg (or .214 mols). Working backwards this means that the starting Z-isomer content was, at most, 90%. That is:

[3] The molecular weight of risperidone is 410.49 and is rounded herein to 410.

0.214 mols risperidone = (% Z-isomer)(94% conversion efficiency)(.2532 mols oxime)

0.214 mols risperidone/(.238) = %Z-isomer

89.9% = Z-isomer

In fact, unlike applicants' Example 8, Olondriz Example 10 uses the stronger (and more dangerous) base of sodium hydride instead of KOH and carries out the reaction for twice as long (one hours versus 30 minutes) at approximately the same temperature (e.g. about 70°C). The efficiency under Olondriz's conditions would not be expected to be lower than Applicants' Example 8, which used a less potent base and half the reaction time. Indeed, Olondriz Example 11, which uses KOH as the base, had an even lower yield of 78.7%.

Importantly, the above assumes that all of the Z-isomer is initially present in calculating the maximum enriched state. But that assumption may not be correct. As taught in the present specification, racemization can occur when the unreactive E-isomer is sufficiently heated. (See Specification at page 10, line 12 *et seq.*). Thus, Z-isomer can be created during the reaction, leading to higher yields without having a higher starting content of Z-isomer. The above 90% Z-isomer enrichment is truly the highest estimate of Z-isomer content, but still falls short of the claimed enrichment of at least 95%.

The fact that the Z-isomer content could not be at least 95% is also seen from the creation of the oxime (7) in Example 9 of Olondriz. The oxime (7) was made by an oximation of the corresponding ketone at reflux for 10 hours. The oximation of the ketone produces a mixture of the E- and Z- isomers of the oxime due to the mechanism of the reaction. Additionally, oximation under long-term heating, as in Example 9, will also

lead to a mixture of isomers. Thus a mixture of E- and Z-isomers of the oxime was produced in the 10 hour reaction of Example 9.

To obtain the oxime (7) in 95% Z-isomer configuration, a resolution step must be performed; e.g., there must be found an oxime derivative that has a different property in E- or Z- conformation to allow separation. In the present invention, this difference was discovered in the acetate salt. There is no such resolution or isolatable derivative mentioned in Example 9 of Olondriz. The oxime was isolated per se, without any resolution means. Recrystallization from ethyl acetate could, in theory, enhance the E/Z ratio (as one of the isomers could be less soluble than the other), but the obtained yield of the recrystallized oxime in the Example 9 (76%) indicates that the compound contained both the E- and Z- isomer. Furthermore, the isolated oxime in Olondriz has a quite broad melting point; a sterically pure oxime would have a narrow melting point, particularly after the recrystallization. From this data there is no basis to assert that Olondriz made the oxime (7) in 95% Z-isomer form. To the contrary, the data indicates that it was not an enriched Z-isomer as per claim 9.

In view of the above comments and the data in the present application and Olondriz, the Examiner has no reasonable basis to assert that Olondriz's Example 10 inherently shows a formula (7) oxime having a Z-isomer content of at least 95% as per claim 9. The Examiner's position is based only on "possibilities,"[4] which are unlikely, if not contrary, in view of the meaningful data of record. Indeed both the formation and use of the oxime (7) confirm that Olondriz could not have had a 95% Z-isomer of oxime (7). Accordingly, the Examiner's rationale fails to establish a prima facie case of inherent

[4] Inherency may not be established by probabilities or possibilities. *In re Robertson*, 169 F.3d 743 (Fed. Cir. 1999).

anticipation of claim 9 over Olondriz's Example 10. Withdrawal of this rejection is respectfully requested.

B. Claims 1-8 would not have been obvious over Strupczewski

Claims 1-8 stand rejected as being obvious under 35 U.S.C. § 103(a) over Strupczewski (U.S. 4,408,054). This rejection is in error and reversal thereof is requested.

Claim 1 recites an acetic acid salt of an oxime of formula (3) or (7). The acetic acid salts of these oximes have been found advantageous in enhancing the Z-isomer content, which in turn leads to higher cyclization efficiency in forming a benzisoxazole ring. The acetic acid salt can work as a resolution agent to separate the Z- and E-isomers and thus obtain an enriched Z-isomer content (such as 95% as claimed in claim 9).

Strupczewski relates to benzisoxazole compounds that have analgesic activity (See Formula 1 and the accompanying text in col. 1). Various synthetic strategies A-G are set forth for making the benzisoxazole compounds. Ketone compounds and corresponding oxime compounds, along with the "salts thereof," are described as "intermediates" for making the benzisoxazole compounds in col. 2 lines 1-63. In addition, the oxime compound formula is claimed in claim 1 of Strupczewski. The oxime compound formula generically encompasses the applicants' claimed specific oxime of formula (3) and "salts thereof."

Example 25 of Strupczewski shows an oxime corresponding to applicants' formula (3) oxime being reacted to further contain an alkenyl substituent on the piperidyl nitrogen. The starting oxime is not a salt, much less the applicants' claimed acetic acid salt. The allylpiperidine oxime product is obtained as the HCl salt, however. While

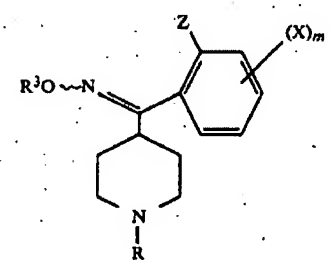
nothing further is done with the allylpiperidine oxime of Example 25, Scheme E in col. 15-16 suggests that such an oxime could be useful for making one of the preferred benzisoxazole analgesics via cyclization.

Recognizing that Strupczewski does not identically describe the acetic acid salt of a compound of formula (3), the Examiner nonetheless asserts that Strupczewski renders the claimed salt compound obvious. The Examiner's rejection fails to provide adequate motivation to render the claimed compound prima facie obvious, and fails to consider the invention as a whole including the unexpected ability of the claimed acetic acid salt to resolve Z- and E-isomers of the oxime. Accordingly, the Examiner's rejection is in error.

No prima facie case of obviousness

The Examiner essentially has two rationales for "finding" the presently claimed oxime salt compound. The first rationale is based on the generic teachings of the oxime compounds in Strupczewski as shown in Strupczewski's claim 1, reproduced below:

1. A compound of the formula



wherein R is hydrogen, loweralkyl, loweralkenyl or a group of the formula

wherein R^1 is hydrogen, loweralkyl or a group of the formula OR^2 wherein R^2 is benzyl; R^3 is hydrogen or a group of the formula

> wherein R^4 is hydrogen, loweralkyl; X is hydrogen, loweralkoxy, loweralkyl, halogen or hydroxy; Z is halogen or hydroxy; m is 1 or 2; the geometric isomers and optical antipodes thereof; or salts thereof where R is hydrogen, loweralkyl or loweralkenyl.

The scope of the oxime compounds embraced by the generic formula is very large, e.g., embracing millions of compounds. Further the preference is not for simple compounds where R is hydrogen, etc., but for more complex compounds where R is alkenyl. This is because the preferred analgesics "are those compounds wherein R is loweralkenyl or cycloalkenylloweralkyl." (col. 1 lines 46-48). Indeed, in reexamination the R group was limited to these more preferred, more complex molecules.

Selecting the applicants' claimed single oxime molecule from the large generic teaching of Strupczewski could not have been prima facie obvious as the Examiner asserts. *In re Baird*, 16 F.3d 380,382-383 (Fed.Cir.1994) ("[a] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds"). As in *Baird*, here the applicants' claim is directed to a single molecule within the vast generic teaching of the prior art reference. And also like *Baird*, the prior art leads away from the selections necessary to arrive at the applicants' claimed molecule. Furthermore, even if all the substituents are correctly selected so as to arrive at applicants' oxime of formula (3), the average artisan would need to additionally select the claimed acetic acid salt from the near infinite genus of all "salts." The description of "salts thereof" is not sufficient to render every salt prima facie obvious. *In re Jones*, 958 F.2d 347, 350 (Fed.Cir.1992).

Recognizing that the scope of "salts thereof" is indeed extremely broad, the Examiner attempts to narrow the scope of the salts by improperly limiting the salts to the exemplified species of pharmaceutically acceptable salts taught for use with the

benzisoxazole analgesic. But the intermediate compounds are not limited to pharmaceutically acceptable salts by the teachings in Strupczewski. The fact that the benzisoxazole final compounds are described as including "pharmaceutically acceptable acid addition salts," while the intermediates were not, indicates that Strupczewski intended the broader genus of "salts" for the intermediates. Accordingly, the scope of salts is not narrow as the Examiner suggests, but quite broad.[5]

In summary, the worker of ordinary skill in the art would not have been motivated to select the particular salt of the particular oxime compound as claimed in applicants' claim 1 from the very large number of different oxime compounds and the near infinite number of possible salts thereof. *Baird; Jones*. Accordingly, selection of the applicants' claimed acetic acid salt of oxime of formula (3) would not have been prima facie obvious.

The Examiner's second rationale is based on Strupczewski Example 25. Specifically, the Examiner asserts that it would have been obvious to modify the oxime starting material shown in Example 25 to be an acetic acid salt and thereby obtain the applicants' claimed invention. But Strupczewski provides no teaching or suggestion for such a modification.

Modifying Example 25 to use the acetic acid salt of the 4-(2,4-diflourobenzoyl)-piperidine oxime (as opposed to the oxime base per se, as written) does not fit in

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[5] Even ignoring the fact that "salts thereof" is not limited in any way, Strupczewski's description of pharmaceutically acceptable benzisoxazole salts is not limited to nine salts as the Examiner suggests. The skilled worker must first choose salts of monobasic carboxylic acids as opposed to salts of mineral acids (such as "hydrochloric acid, sulfuric acid, nitric acid, and the like"), salts of dibasic carboxylic acid salts (such as "maleic acid, fumaric acid, and the like"), and salts of tribasic carboxylic acids (such as "carboxysuccinic acid, citric acid, and the like"), all of which are taught as pharmaceutically acceptable salts in Strupczewski. Then the skilled worker must choose acetic acid as opposed to "propionic acid and the like," i.e., as opposed to propionic acid, formic acid, butyric acid, valeric acid, caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, lauric acid, or stearic acid. This is hardly choosing from a group of only 9 members, as suggested by the Examiner.

Example 25's reaction scheme. The acetic acid salt would introduce a competing counter-ion to the desired hydrochloride salt of the product; i.e., interfering with the stated goal of forming the 4-(2,4-Difluorobenzoyl)-1-allylpiperidine oxime *hydrochloride*. Besides apparently being counter-productive to the intended reaction, the Examiner has failed to offer any reason for changing the starting oxime from a base to a salt form. The fact that one could do something, in hindsight, does not make it obvious to have done so. *In re Gordon,* 733 F.2d 900, 902 (Fed.Cir.1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification").

Other than merely locating the words "acetic acid" and "salt" in Strupczewski, the Examiner has failed to provide any suggestion or motivation in the prior art for a skilled worker to modify Example 25's oxime intermediate base to be a salt of acetic acid. But demonstrating that salts of acetic acid are known is not enough to establish obviousness. "As is clear from cases such as [*United States v. Adams*, 383 U.S. 39 (1966)], a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007).

Accordingly, based on the broad generic teaching and/or Example 25, Strupczewski does not render claims 1-8 prima facie obvious. Reversal of the rejection is warranted on this basis alone.

Failure to consider unexpected properties

Moreover, even assuming, *arguendo*, that the Examiner has established a prima facie case of obviousness, the unexpectedly superior properties of the claimed acetic acid

salt of the oxime compound of formula (3) establishes non-obviousness. The acetic acid salt of oxime (3) can resolve the geometric isomers Z and E. This is shown in Examples 1 and 2 of the instant specification. Nothing in Strupczewski teaches or suggests this unusual and advantageous property. Indeed, while Strupczewski appreciated that Z- and E-isomers existed (see col. 3), Strupczewski did not teach the desirability of resolving the Z-isomer or that a salt of the oxime (3) can separate the Z- and E-isomers, much less that the acetic acid salt is the one to use. But rather applicants discovered that an acetic acid salt of the Z-isomer oxime of formula (3) (or (7)) can be preferentially precipitated from a solution containing a mixture of the Z- and E-isomer oximes. In this way, the acetic acid salt enables the formation of a Z-isomer enriched oxime of formula (3)(or (7)), which in turn improves the oximes' reactivity in the subsequent cyclization reaction. Thus, the claimed acetic acid salt is a more useful intermediate in making, e.g., risperidone, than the unresolved corresponding free base. These unexpected properties (i.e., acetic acid salt serving as a resolving agent and forming crystals) provide tangible advantages and yet these properties are not taught or suggested in Strupczewski.

The Examiner does not allege that the properties are expected from the teachings in Strupczewski, or that the properties are not significant. Instead, the Examiner ignores the unexpected results in her obviousness analysis. Such an analysis is plain error. In view of the unexpectedly superior results, e.g. the ability to resolve Z-isomer, the claimed acetic acid salt of oxime (3) and (7) could not have been obvious to the worker of ordinary skill in the art at the time the invention was made.

Accordingly, claims 1-8 could not have been obvious over Strupczewski within the meaning of 35 U.S.C. § 103. Reversal of this rejection is respectfully requested.

C. Claims 6-8 would not have been obvious over Strupczewski

In addition to the above arguments, claims 6-8 are clearly not rendered obvious by the teachings in Strupczewski. Specifically, claims 6-8 are limited to the oxime of formula (7). Strupczewski does not teach or suggest a compound of formula (7). Note that the R group in Strupczewski does not include a pyrido-pyrimidinone group as per formula (7) and risperidone. Indeed, the analgesic benzisoxazoles of Strupczewski do not include risperidone, the target benzisoxazole of the present application, precisely because the substituent group on the piperidyl nitrogen is different. Having failed to teach or suggest the applicants' oxime of formula (7), Strupczewski likewise fails to teach or suggest an acetic acid salt thereof. Accordingly, claims 6-8 are further patentably distinguished because Strupczewski does not teach or suggest the claimed acetic acid salt of the oxime of formula (7).

D. Claims 4 and 5 would not have been obvious over Strupczewski

Claims 4 and 5 are also further patentably distinct. These claims recite that more Z-isomer is present than E-isomer (claim 4) and that the oxime salt is 90% Z-isomer (claim 5). The Examiner failed to specifically address the individual limitations recited in instant claims 4 and 5. Strupczewski does not teach or suggest containing more or less of one isomer over the other and clearly does not teach or suggest having 90% Z-isomer.

Perhaps the Examiner believed that these relationships were inherent. The Examiner states that the oxime of Example 25 "is used for the same utility" as in the present application, namely "the synthesis of risperidone" and that the same subsequent sequence of reactions are used citing to Strupczewski Example 26. But, Strupczewski does not make risperidone and Example 26 does not use the product of Example 25.

Nonetheless, the Examiner concludes that "[t]his heating does the enrichment." But the present application teaches that heating causes racemization, not resolution. The Examiner's basis to reject these dependent claims is indiscernible and in any event not supported by Strupczewski. Accordingly, claims 4 and 5 are further patentably distinct.

VIII. Conclusion

For the reasons set forth above, each of the Examiner's rejections is in error and reversal thereof is respectfully requested.

Respectfully submitted,

Date: 11/5/2007 (Monday)

By: _____

Mark R. Buscher
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Suite 202
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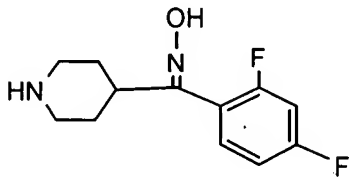
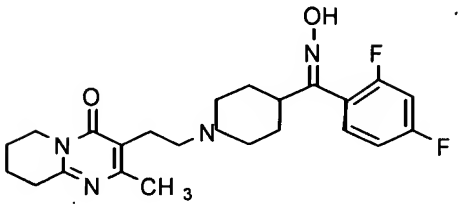
Claims Appendix

1. (Original) An acetic acid salt of a compound of formula (3) or (7):



(3)



(7)

2. (Original) The acetic acid salt according to claim 1, wherein said salt is in solid form.

3. (Original) The acetic acid salt according to claim 1, wherein said salt is the salt of said compound of formula (3).

4. (Original) The acetic acid salt according to claim 3, wherein said salt contains more of the Z-isomer of formula (3) than of the E-isomer of formula (3).

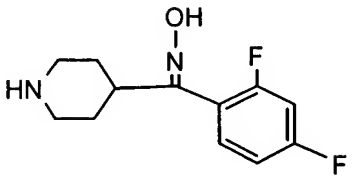
5. (Original) The acetic acid salt according to claim 4, wherein said salt is in solid form and is at least 90% isomerically pure Z-isomer of formula (3).

6. (Original) The acetic acid salt according to claim 1, wherein said salt is the salt of said compound of formula (7).

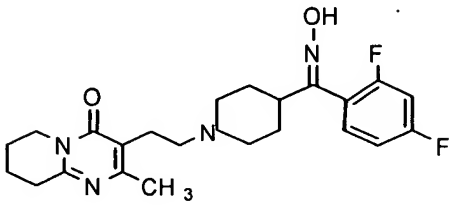
7. (Original) The acetic acid salt according to claim 6, wherein said salt contains more of the Z-isomer of formula (7) than of the E-isomer of formula (7).

8. (Original) The acetic acid salt according to claim 7, wherein said salt is in solid form and is at least 90% isomerically pure of Z-isomer of formula (7).

9. (Previously Presented) An enriched Z-isomer oxime of formula (3) or (7):



(3)



(7)

wherein the amount of Z-isomer is at least 95%, based on the total amount of said oxime.

10. (Cancelled)

11. (Cancelled)

12. (Original) The enriched Z-isomer according to claim 10, wherein said oxime is a compound of formula (3).

13. (Original) The enriched Z-isomer according to claim 10, wherein said oxime is a compound of formula (7).

14-39. (Cancelled).

Evidence Appendix

(NONE)

Related Proceedings Appendix

(NONE)